

Applicants: James M. Binley et al.  
Serial No.: 10/780,993  
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Page 3

Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims

87-93, 95-113, 126-132, 134-152

Claims 1-86. (Canceled)

O.K. ✓ 87. (Currently Amended) A DNA which upon transcription produces an RNA encoding a modified HIV-1 gp140 polypeptide of an HIV-1 isolate, which polypeptide upon cleavage produces a modified gp120 and a modified gp41 ectodomain ~~of gp41~~ which together form a complex, said complex (i) exhibiting enhanced binding to HIV-1 neutralizing antibodies and reduced binding to HIV-1 non-neutralizing antibodies, wherein the modified gp120 modifications comprises an A492C mutation in gp120 and the modified gp41 ectodomain comprises a T596C mutation in gp41, said mutations being numbered by reference to the HIV-1 isolate JR-FL, and (ii) permitting the formation of ~~resulting in~~ a disulfide bond between the modified gp120 and the modified gp41 ectodomain gp41 which stabilizes the complex ~~otherwise non-covalent gp120-gp41 interaction~~.

✓ 88. (Previously Presented) The DNA of claim 87, wherein the HIV-1 isolate represents a subtype selected from the group consisting of clades A, B, C, D, E, F, G, H and O.

✓ 89. (Previously Presented) The DNA of claim 88, wherein the HIV-1 isolate is HIV-1<sub>JR-FL</sub>, HIV-1<sub>DH123</sub>, HIV-1<sub>GUN-1</sub>, HIV-1<sub>89.6</sub> or HIV-1<sub>HXB2</sub>.

✓ 90. (Previously Presented) The DNA of claim 87, wherein the

modified gp120 is further characterized by the absence of one or more of the variable loops present in unmodified gp120.

- ✓91. (Previously Presented) The DNA of claim 90, wherein the absent variable loop comprises V1, V2, V3 or a combination thereof.
- ✓92. (Previously Presented) The DNA of claim 90, wherein the absent variable loop comprises V1 and V2.
- ✓93. (Currently Amended) The DNA of claim 87, wherein the modified gp120 is further characterized by the ~~absence or~~ presence of one or more canonical glycosylation sites ~~present or absent, respectively,~~ in unmodified gp120..
- ✓94. (Canceled)
- ✓95. (Previously Presented) The DNA of claim 87, which is cDNA or genomic DNA.
- ✓96. (Currently Amended) The DNA of claim 87, wherein the DNA ~~codon usage~~ is optimized ~~within said DNA~~ to enhance the translation of codons in mammalian cells.
- ✓97. (Previously Presented) A non-replicating viral vector comprising the DNA of claim 87.
- ✓98. (Previously Presented) A replicable vector comprising the DNA of claim 87.
- ✓99. (Previously Presented) The replicable vector of claim 98, wherein the vector is a plasmid, cosmid, virus, viral

vector,  $\lambda$  phage or YAC.

✓100. (Previously Presented) The replicable vector of claim 98, wherein the vector is a plasmid.

✓101. (Previously Presented) The replicable vector of claim 99, wherein the vector is a viral vector.

✓102. (Previously Presented) A replicable vector comprising the DNA of claim 87, wherein the modified gp120 is further characterized by the absence of one or more of the variable loops present in unmodified gp120.

✓103. (Previously Presented) The replicable vector of claim 102, wherein the absent variable loop comprises V1, V2, V3 or a combination thereof.

✓104. (Currently Amended) The replicable vector of claim 102, wherein the absent variable loop comprises V1 and V2.

101 - 105. (Previously Presented) A host cell comprising the vector of claim 98.

101 - 106. (Currently Amended) The host cell of claim 105, which is a eukaryotic cell.

101 - 107. (Currently Amended) The host cell of claim 106, which is a mammalian cell.

✓108. (Currently Amended) The host cell of claim 107, which is a Chinese hamster ovary (CHO) cell.

✓109. (Currently Amended) The host cell of claim 105, which is a

bacterial cell.

101

110. (Currently Amended) The host cell of claim 105, further comprising a vector which expresses an endoprotease of the furin family.

✓ 111. (Previously Presented) A composition comprising the DNA of claim 87.

✓ 112. (Previously Presented) The composition of claim 111, wherein the composition comprises the DNA in a DNA plasmid, a replicating viral vector, or a non-replicating viral vector.

113. (Previously Presented) The composition of claim 112, further comprising an adjuvant.

114-125. (Canceled)

126. (Currently Amended) A DNA which upon transcription produces an RNA encoding a modified HIV-1 gp140 polypeptide of an HIV-1 isolate, which polypeptide upon cleavage produces a modified gp120 and a modified gp41 ectodomain ~~of gp41~~ which together form a complex, said complex (i) exhibiting enhanced binding to HIV-1 neutralizing antibodies and reduced binding to HIV-1 non-neutralizing antibodies, wherein the modified gp120 ~~modifications~~ comprises a ~~mutation in gp120 selected from the group consisting of~~ V35C mutation, a Y39C mutation, a W44C mutation, a P484C mutation, a G486C mutation, a A488C mutation, a P489C mutation, a T490C mutation, or a and A492C mutation and a ~~mutation in ectodomain gp41 selected from the group consisting of~~ the modified gp41 ectodomain comprises a

D580C mutation, a W587C mutation, a T596C mutation, a V599C mutation, a P600C mutation, or a ~~and~~ W601C mutation, said mutations being numbered by reference to the HIV-1 isolate JR-FL, and (ii) permitting formation of ~~resulting in~~ a disulfide bond between the modified gp120 and the modified gp41 ectodomain ~~gp41~~ which stabilizes the complex ~~otherwise non-covalent gp120-gp41 interaction~~.

- ✓ 127. (Previously Presented) The DNA of claim 126, wherein the HIV-1 isolate represents a subtype selected from the group consisting of clades A, B, C, D, E, F, G, H and O.
- ✓ 128. (Previously Presented) The DNA of claim 127, wherein the HIV-1 isolate is HIV-1<sub>JR-FL</sub>, HIV-1<sub>DH123</sub>, HIV-1<sub>GUN-1</sub>, HIV-1<sub>89.6</sub> or HIV-1<sub>HXB2</sub>.
- ✓ 129. (Previously Presented) The DNA of claim 126, wherein the modified gp120 is further characterized by the absence of one or more of the variable loops present in unmodified gp120.
- ✓ 130. (Previously Presented) The DNA of claim 129, wherein the absent variable loop comprises V1, V2, V3 or a combination thereof.
- ✓ 131. (Previously Presented) The DNA of claim 129, wherein the absent variable loop comprises V1 and V2.
- ✓ 132. (Currently Amended) The DNA of claim 126, wherein the modified gp120 is further characterized by the ~~absence or~~ presence of one or more canonical glycosylation sites ~~present or absent, respectively,~~ in unmodified gp120.

Applicants: James M. Binley et al.  
Serial No.: 10/780,993  
Filed: February 18, 2004  
Page 8

- ~~133~~. (Canceled)
- ✓134. (Previously Presented) The DNA of claim 126, which is cDNA or genomic DNA.
- ✓135. (Currently Amended) The DNA of claim 126, wherein the DNA ~~codon usage~~ is optimized within ~~said DNA~~ to enhance the translation of codons in mammalian cells.
- ✓136. (Previously Presented) A non-replicating viral vector comprising the DNA of claim 126.
- ✓137. (Previously Presented) A replicable vector comprising the DNA of claim 126.
- ✓138. (Previously Presented) The replicable vector of claim 137, wherein the vector is a plasmid, cosmid, virus, viral vector,  $\lambda$  phage or YAC.
- ✓139. (Previously Presented) The replicable vector of claim 137, wherein the vector is a plasmid.
- ✓140. (Previously Presented) The replicable vector of claim 138, wherein the vector is a viral vector.
- ✓141. (Previously Presented) A replicable vector comprising the DNA of claim 126, wherein the modified gp120 is further characterized by the absence of one or more of the variable loops present in unmodified gp120.
- ✓142. (Previously Presented) The replicable vector of claim 141, wherein the absent variable loop comprises V1, V2, V3 or a

combination thereof.

✓ 143. (Currently Amended) The replicable vector of claim 141, wherein the absent variable loop comprises V1 and V2.

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144. (Previously Presented) A host cell comprising the vector of claim 137.

145. (Currently Amended) The host cell of claim 144, which is a eukaryotic cell.

146. (Currently Amended) The host cell of claim 145, which is a mammalian cell.

✓ 147. (Currently Amended) The host cell of claim 146, which is a Chinese hamster ovary (CHO) cell.

✓ 148. (Currently Amended) The host cell of claim 144, which is a bacterial cell.

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149. (Currently Amended) The host cell of claim 144, further comprising a vector which expresses an endoprotease of the furin family.

150. (Previously Presented) A composition comprising the DNA of claim 126.

151. (Previously Presented) The composition of claim 150, wherein the composition comprises the DNA in a DNA plasmid, a replicating viral vector, or a non-replicating viral vector.

152. (Previously Presented) The composition of claim 150,

Applicants: James M. Binley et al.  
Serial No.: 10/780,993  
Filed: February 18, 2004  
Page 10

further comprising an adjuvant.

153-158. (Canceled)